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Vision Research 45 (2005) 1471–1479

Vision Research

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Spatial interactions in amblyopia: Effects of stimulus parameters and amblyopia type

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Received 7 April 2004; received in revised form 25 November 2004

Abstract

Adults with amblyopia were recently shown to perform abnormally in tasks requiring integration of local features into global percepts. Moreover, spatial interactions in amblyopic patients, though often found to be abnormal, showed marked variability. Here we measured collinear lateral interactions using Gabor patches in a large number of amblyopic ($N = 75$) and normal subjects ($N = 25$), testing four spatial frequencies (1.5, 3, 6, 9 cpd). We used the lateral masking paradigm, in which the contrast-detection threshold is measured in the presence of high-contrast flankers at different distances from a central target. Whereas in normal subjects spatial interaction patterns were evident across all spatial frequencies, amblyopic subjects showed abnormal spatial interactions and increasing deficiencies with increasing spatial frequencies. These abnormalities depended on the axis of astigmatism (in meridional amblyopia) and were more pronounced in strabismic than in anisometropic amblyopia. Spatial interactions were independent on the contrast-detection thresholds. Thus, adults with amblyopia might perform as well as normal observers for some stimulus parameters and abnormally for others. Our results indicate a close relationship between abnormal visual input to the visual cortex during development and abnormal functionality of the collinear spatial interactions in adults with amblyopia.

Keywords: Amblyopia; Spatial interaction; Lateral interaction; Facilitation; Suppression

1. Introduction

The contrast response function of individual neurons is thought to be determined by feed-forward mechanisms that process local stimulus attributes. A number of recent studies have demonstrated, however, that the contrast response is also determined by global aspects of the visual stimulus (context) and can be modulated by remote images in the visual field. The context effect has been demonstrated in psychophysical studies (Bonneh & Sagi, 1998; Polat & Sagi, 1993; Polat & Sagi, 1994a; Polat & Sagi, 1994b; Solomon & Morgan, 2000; Woods, Nugent, & Peli, 2002), in visual evoked potentials (Polat & Norcia, 1996, 1998), and in single-unit recordings in cats and monkeys (Crook, Engelmann, & Lowel, 2002; Kapadia, Ito, Gilbert, & Westheimer, 1995; Kasamatsu, Polat, Pettet, & Norcia, 2001; Levitt & Lund, 1997; Mizobe, Polat, Pettet, & Kasamatsu, 2001; Polat, Mizobe, Pettet, Kasamatsu, & Norcia, 1998; Sengpiel, Baddeley, Freeman, Harrad, & Blakemore, 1998; Sillito, Grieve, Jones, Cudeiro, & Davis, 1995).

Facilitation of the contrast threshold by spatial context occurs preferentially with collinear flankers (Polat & Sagi, 1993; Polat & Sagi, 1994a; Polat & Sagi, 1994b), suggesting that contrast might be summating preferentially along the collinear configurations at threshold (Polat, 1999). This finding is consistent with an elongated summation field along the collinear

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0042-6989/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.visres.2004.12.014

direction (Chen & Tyler, 1999; Polat & Norcia, 1998; Polat & Tyler, 1999), and might be mediated by the collinear long-range interactions that connect receptive fields along their optimal orientations (Kasamatsu et al., 2001; Polat, 1999; Polat et al., 1998).

In subjects with amblyopia there are deficiencies of the best-corrected visual acuity and other visual functions (for reviews see (Greenwald & Parks, 1999; Hess, Field, & Watt, 1990; Levi, 1991)) as a result of abnormal visual processing, which cannot be attributed directly to any structural abnormality of the eye.

In most amblyopic eyes abnormal contrast-sensitivity function is observed mainly at high spatial frequencies, with little or no loss of contrast sensitivity at low spatial frequencies (Gstalder & Green, 1971; Harwerth & Levi, 1977). It is assumed that CSF is determined solely by feed-forward inputs to first-order localized filters. Thus, the extent of contrast-sensitivity loss in amblyopia depends on the functionality of the first-order filters, which in amblyopia might be normal but suffer from reduced sensitivity (Ellemberg, Hess, & Arsenault, 2002; Hess, 1980; Hess & Campbell, 1980).

Recent studies indicate, however, that amblyopic subjects exhibit abnormalities in tasks requiring cooperation among the local mechanisms (Kovács, Polat, Pennefather, Chandna, & Norcia, 2000; Mussap & Levi, 2000; Polat, Ma-Naim, Belkin, & Sagi, 2004; Polat, Sagi, & Norcia, 1997; Popple & Levi, 2000). Indications of abnormal function came from the observed failure of amblyopic subjects to display normal collinear facilitation in psychophysical experiments and studies of visual evoked potential (Polat et al., 1997). Some subjects even showed suppression instead of facilitation. Studies demonstrated abnormalities in performance of a contour integration task assumed to involve lateral interactions (Chandna, Pennefather, Kovács, & Norcia, 2001; Kovács et al., 2000). Other studies showed, however, that only individuals with strabismic amblyopia failed on such tasks (Hess & Demanins, 1998; Hess, McIlhagga, & Field, 1997). Support for abnormalities in integrative processes rather than at the local level came from the finding that amblyopic subjects showed deficits in a task requiring detection of targets composed of large numbers of dots (Mussap & Levi, 2000). In another study, measurement of the tilt illusion showed that whereas normal observers see illusory tilt, amblyopic subjects see true alignment (Popple & Levi, 2000). Recently, amblyopic subjects were found to show compromised lateral interactions while performing lateral masking task with collinear Gabor patches (Levi, Hariharan, & Klein, 2002) similar to the one employed by Polat et al. (1997). Thus, there is growing support for the idea that in amblyopic subjects, spatial interactions are compromised. However, the effect of abnormality does not appear to be similarly expressed in all amblyopic subjects (Levi et al., 2002).

A critical problem with amblyopia research is the small population size generally tested in each study. Given the large variability among individuals, as expected with abnormal functions, reliable conclusions are difficult to draw. Here we measured lateral interactions, using Gabor patches, across four spatial frequencies and four orientations, in a large number of amblyopic subjects ($N = 75$). We found that deficiencies in lateral interactions increased with increasing spatial frequency, depend on the axis of astigmatism, and was more pronounced in strabismic than in anisometropic amblyopia. Thus, individual amblyopic subjects might perform normally with one set of stimulus parameters and abnormally with another.

2. Methods

The study population comprised subjects aged between 9 and 55 years, who had been diagnosed with unilateral amblyopia secondary to strabismus ($n = 38$) or anisometropia ($n = 37$) and had a best corrected visual acuity (measured on LogMar charts, ETDRS) of 6/9 to 6/30 in the amblyopic eye. The mean VA was 0.39 ± 0.025 LogMar (mean ± SEM) for the anisometropic subjects and 0.44 ± 0.02 LogMar for the strabismic subjects (see Fig. 1 for the distribution of the VA). Each subject (or parent/legal guardian) signed an informed consent form approved by the local Institutional Review Board. A total of 75 amblyopic subjects and 25 subjects with normal vision participated in the study.

The stimuli were localized gray level gratings (Gabor patches) with spatial frequencies of 1.5, 3, 6 and 9 cycles per degree (cpd) modulated from a background luminance of 40 cd m^{-2} (Fig. 2).

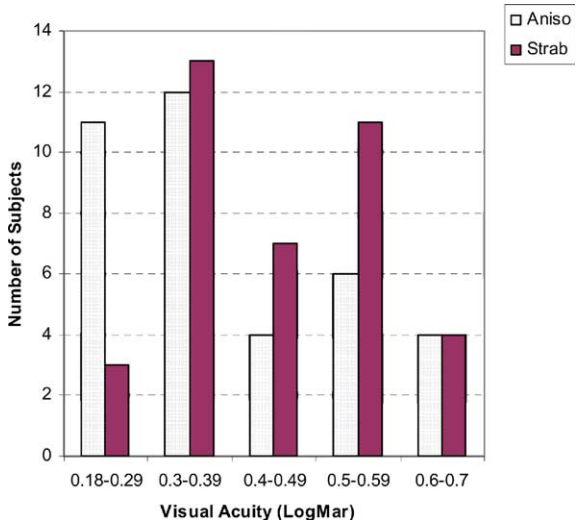

Fig. 1. Histogram of the visual acuity (VA, LogMar) for anisometropic (Aniso, dotted bars) and strabismic amblyopes (filled bars). The average VA of anisometropic was 0.39 ± 0.02 (means ± SEM) and strabismic 0.44 ± 0.02.

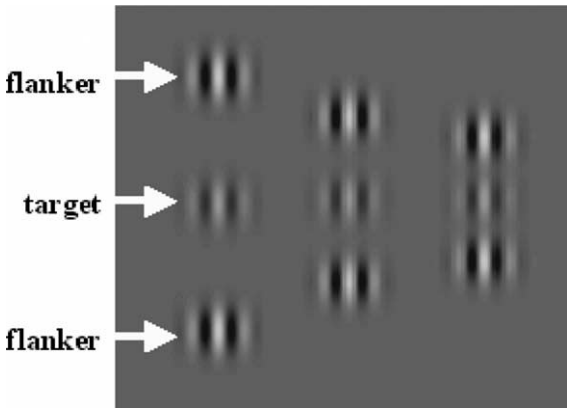

Fig. 2. Example of stimuli used in this study. Three configurations of target and flankers used in the lateral interaction experiments with varying target–flanker separations: 1.5λ, 3λ and 6λ (wavelengths).

Stimuli were presented on a Philips multiscan 107P color monitor, using a PC system. The effective size of the monitor screen was 24×32 cm, which at a viewing distance of 150 cm subtends a visual angle of $9 \times 12°$. Subjects' responses were recorded in a dark cubicle, where the only ambient light came from the display screen.

The contrast threshold was measured by a procedure in which the subject was required to choose between two temporal alternatives. Two images were presented, each for 80, 160 or 320 ms (see below), with an interval of 500 ms between them. The subjects, seated 1.5 m from the screen wearing their best optical correction with the non-amblyopic eye occluded, were required to detect the target, which was shown in only one of the two presentations. A visible fixation circle indicated the location of the target between presentations. Subjects activated the presentation of each pair of images at their own pace. They were informed of a wrong answer by an auditory feedback after each pair of presentations.

The lateral interactions and contrast detection tasks using Gabor patches (see Fig. 2) were similar to those described by Polat and Sagi (1993, 1994a, 1994b), and included target detection with and without flanking collinear patches with contrast five times above the contrast threshold of the target. In each session only one configuration (spatial frequency and orientation) was tested. Contrast thresholds were measured utilizing a staircase method, which was shown to converge to 79% correct (Levitt, 1971). In this method, the target contrast is increased by 0.1 log units (26%) after an erroneous response and decreased by the same amount after three consecutive correct responses. About 40–50 trials were needed to estimate the threshold in each block.

The sizes (spatial frequencies), orientations and the duration of the stimuli were chosen for each of the subjects based on their own performance. The first few sessions were devoted for training and to estimate the contrast sensitivity and the least suppressive meridian. The latter was chosen as the first axis for measurement of the spatial interactions. The selected spatial frequency used to test was the highest spatial frequency that did not exceed twice the mean value of the contrast threshold of that spatial frequency in the normal subjects. If the contrast threshold was too high, the duration increased from 80 to 160 or 320 ms to reach this criterion. The durations was 187 ± 26 (mean $\pm$ se, $n = 6$) for 1.5 cpd; 185 ± 22 for 3 cpd ($n = 19$); 193 ± 16 for 6 cpd ($n = 37$) and 234 ± 31 for 9 cpd ($n = 13$). The average spatial frequency was 4.9 ± 0.37 for the anisometropic and 5.9 ± 0.36 for the strabismic amblyopes. The subjects with normal vision were tested in one spatial frequency 5.9 ± 0.5 ($n = 25$) and the distribution of the spatial frequencies was similar to the amblyopic subjects (see Fig. 5). The reported data (except for data described in Fig. 3) are from the first sessions in which subjects

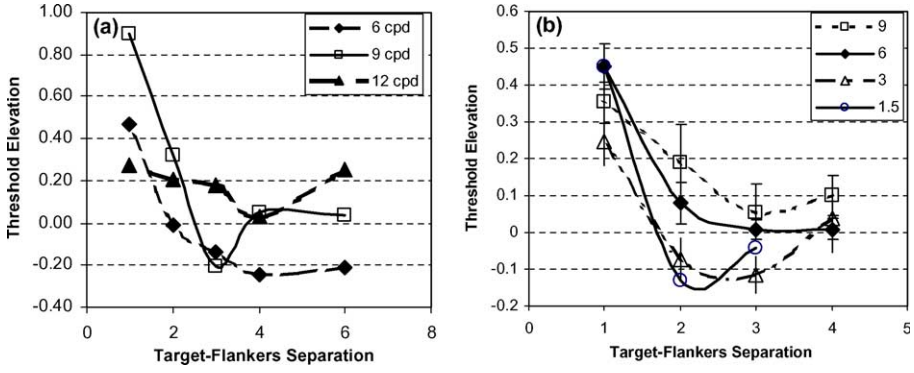

Fig. 3. Example of spatial interactions of an amblyopic subject. (a) Spatial interaction functions in an amblyopic subject (SJ) measured at 6 (filled diamonds), 9 (open squares), and 12 (filled triangles) cpd. Facilitation is indicated by values below zero, and suppression by values above zero. Facilitation decreases with increasing spatial frequencies and is replaced by suppression at 12 cpd. (b) Spatial interaction functions in amblyopic subjects. The figure shows the data set of the initial measurement of lateral interactions in amblyopic subjects (see Section 2). The presented results are means $\pm$ SEM across subjects. Amblyopic subjects show, on average, significant facilitation for 1.5 ($n = 6$) and 3 cpd ($n = 19$) and suppression at 2–3λ with 6 ($n = 37$) and 9 cpd ($n = 13$).

performed the lateral masking task. This was done to avoid the confounding effects of perceptual learning, which improves visual performance (Polat, in press; Polat et al., 2004).

3. Results

3.1. Effect of spatial frequency

Fig. 3a presents the lateral masking function for the amblyopic eye of an anisometropic subject for three different spatial frequencies that were measured. For the lowest spatial frequency (6 cpd, filled diamonds), the function is fairly typical (Polat & Sagi, 1993; Polat & Sagi, 1994a; Polat & Sagi, 1994b), namely facilitation where the distance between target and flanker is greater than 2λ and suppression where the distance is smaller (1λ). With increasing spatial frequencies, however, the facilitation decreased and the suppression increased. Fig. 3b presents the average results across spatial frequencies for all subjects in the amblyopic group. The facilitatory effect in the spatial interactions of subjects in the amblyopic group ($n = 75$) is spatial frequency dependent. The average result of the subjects who were tested at the lower spatial frequencies (1.5 and 3 cpd, $n = 6$ and 19 correspondingly) show some facilitation at 3λ but the average result of the subjects who were tested at the higher spatial frequencies (6 and 9 cpd, $n = 37$ and 13 correspondingly) did not show facilitation but have showed some suppression instead. Thus, amblyopic individuals might show some facilitation and less abnormality at the lower spatial frequencies.

3.2. Comparison between categories and spatial frequencies

To determine whether subjects with strabismic and anisometropic amblyopia differ in their spatial interactions, we divided the amblyopic subjects into two subgroups, those with strabismic amblyopia ($n = 38$) and those with anisometropic amblyopia ($n = 37$). Fig. 4a shows the averaged lateral interaction curves for control group, anisometropic (open circles) and strabismic (open triangle) amblyopia. For the control group (mean spatial frequency ± SEM = 5.9 ± 0.5 cpd; $n = 25$), the spatial interactions curve is typical, showing facilitation at target–flankers separation of $2–4\lambda$. The average data for subjects with anisometropia show reduced facilitation. Strabismic amblyopia exhibited more abnormalities in spatial interactions than those with anisometropic amblyopia and the collinear facilitation was always missing, while suppression was always evident at $2–4\lambda$. To quantify the facilitatory effect we calculated the average of the threshold elevations (log(target threshold alone/target threshold + flakers)) for 2λ, 3λ, and 4λ (Fig. 4b). Subjects with anisometropic amblyopia exhibited significant facilitation that was about half of the control group, but the strabismic group showed suppression. The difference of spatial interactions between the anisometropic and strabismic group is highly significant ($p = 0.001$, t-test).

In order to see the individual differences among subjects we plotted the results of each subject in Fig. 5. To quantify the effect of facilitation as a function of spatial frequency, we calculated the average of the threshold elevation values between 2λ and 4λ for every individual. These results are presented in Fig. 5a. While the data

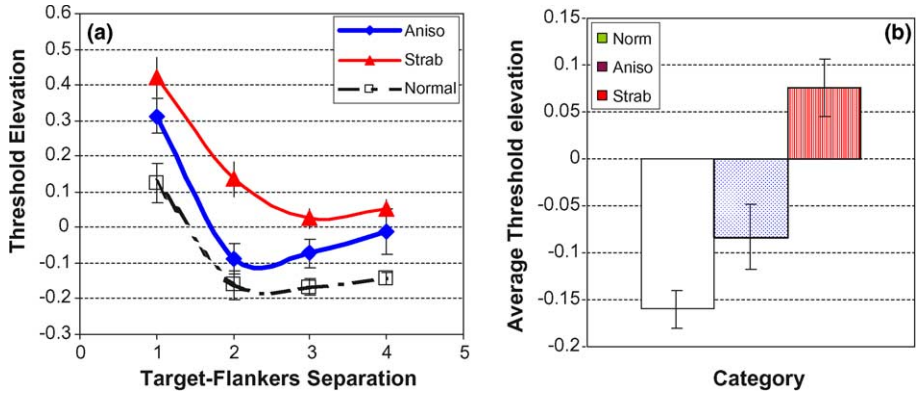

Fig. 4. Spatial interactions of amblyopic and non-amblyopic subjects. (a) Spatial interaction functions in amblyopic subjects. The figure shows the data set of the initial measurement of lateral interactions in amblyopic subjects (see Section 2). The presented results are means ± SEM across subjects. Normal subjects, $n = 25$, average spatial frequency 5.9 ± 0.5; strabismic group, ($n = 38$, average spatial frequency 5.9 ± 0.36); anisometropic group ($n = 37$ average spatial frequency 4.9 ± 0.37). Subjects in anisometropic group show, on average, facilitation but the strabismic group show suppression at $2–3\lambda$. The anisometropic subjects show, on average, less facilitation than normal subjects but the strabismic group show more suppression. (b) The data represents the averaged of the threshold elevation values at 2λ, 3λ, and 4λ. (for 1.5 cpd the 4λ data could not be measured) in amblyopic and control subjects at each spatial frequency tested for the three groups. Negative values indicate facilitation and positive values suppression.

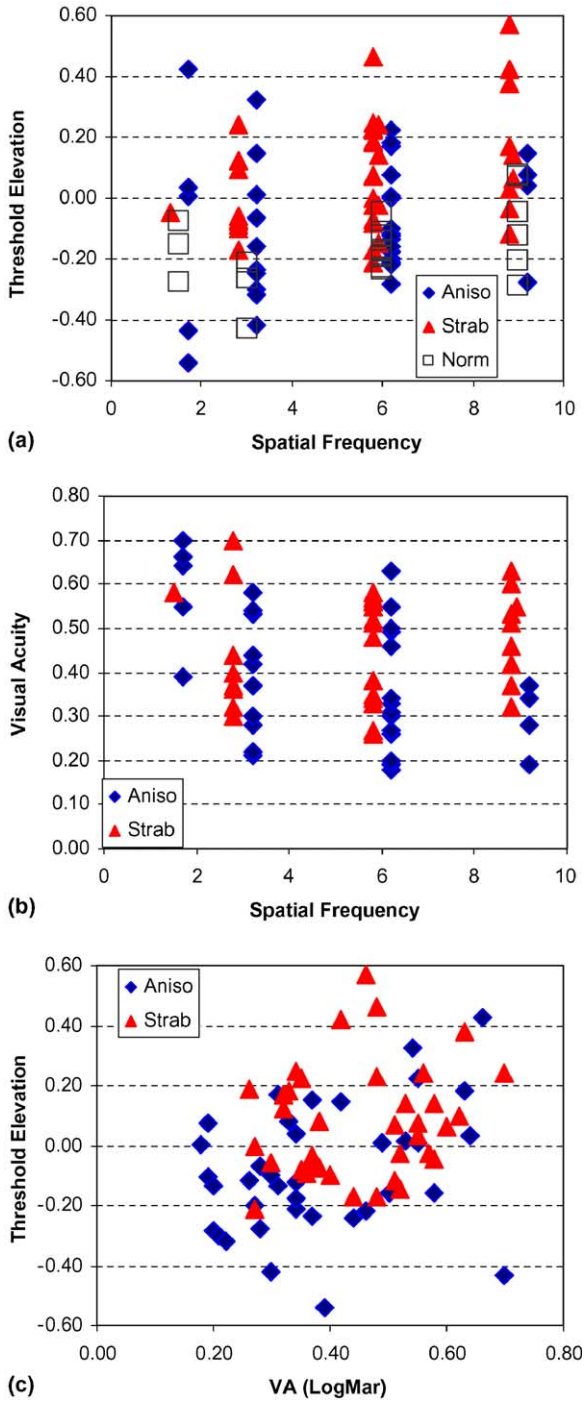

Fig. 5. Relationships between threshold elevation, visual acuity and spatial frequency. (a) The data shows the scatter of the threshold elevation against the spatial frequency of each amblyopic subject (aniso, filled diamond; strab, filled triangle) and control subjects (open squares). Each data point represents one subject. Negative values indicate facilitation and positive values suppression. (b) Scatter plot of the visual acuity (VA) against spatial frequency. The symbols are the same as above. The scatter of the spatial frequency between the two groups was not significantly different ($p = 0.06$, t-test). (c) Distribution of the average threshold elevation values (from Fig. 5a) against VA (LogMar, from Fig. 5b). The symbols are the same as above. The correlation found between VA and threshold elevation was small ($r = 0.32$ for the anisometropic and 0.19 for the strabismic amblyopes).

points of 24 out of 25 of the control subjects (open squares) were distributed below zero (facilitation) the amblyopic subjects showed either facilitation or suppression. However, more anisometropic subjects showed facilitation than strabismic subjects. The difference between the two groups is highly significant ($p < 0.001$, t-test). Even though there were more anisometropic subjects tested at the lower spatial frequency (1.5 cpd) and more strabismic subjects at the high spatial frequency (9 cpd) the distribution of the spatial frequencies among the two amblyopic groups was not significantly different ($p = 0.062$, t-test) thus the difference in threshold elevation cannot be attributed to difference in the tested spatial frequencies.

The average VA of the anisometropic group was 0.39 ± 0.24 LogMar and for the strabismic group 0.44 ± 0.2 LogMar. Thus, the distribution of the VA between the two groups was slightly different ($p = 0.042$, t-test). However, the difference in the threshold elevation cannot be attributed to the small difference in the VA. Fig. 5b shows the scatter plot of the subjects as a function of spatial frequency. There was a tendency for subjects that were tested with low spatial-frequencies to have higher VA. This behavior is specific for the anisometropic subjects ($r = 0.48$) and is absent for strabismic subjects ($r = 0.1$). Note that a correlation here is not unexpected as subjects were assigned to spatial-frequency according to their contrast detection thresholds (see Section 2), thus subjects at lower spatial-frequencies have lower sensitivity at higher frequencies, relative to subjects assigned to the higher-frequencies. The strabismic data deviates from the expected correlation, showing no dependence of VA on spatial-frequency. To directly test the correlation between threshold elevation and VA, we contrasted these two measurements in Fig. 5c. The results show low correlation values between VA and threshold elevation for the two groups ($r = 0.32$ for the anisometropic group and 0.19 for the strabismic group).

In summary, the spatial interactions in amblyopia are abnormal, but are significantly more affected in the strabismic group (Fig. 4, $p = 0.001$, t-test). The results cannot be attributed to differences in contrast sensitivity between the subgroups of amblyopia since they were not very different (strabismic group, average target threshold 9.2 ± 1.3; anisometropic group average target threshold 7.2 ± 1; $p = 0.15$, t-test).

3.3. Meridional amblyopia

The optical error of many amblyopic individuals includes astigmatic error. Uncorrected astigmatic refractive error of more than 1.5 diopters during childhood typically results in development of meridional amblyopia (Greenwald & Parks, 1999). Even after optical correction, contrast sensitivity in adults with amblyopia is

decreased along the higher optical axis (Freeman, 1975; St John, 1997), an effect that is not due to retinal blur (Freeman, 1975; Mitchell, Freeman, Millodot, & Haegerstrom, 1973). To examine whether lateral interactions are more severely abnormal at the axis of higher optical error (astigmatic), we analyzed spatial interactions as a function of the higher and the lower optical blur axes. Included in the analysis were amblyopic subjects in whom the astigmatic error was at least 1.5 diopters (mean ± SEM, 2.7 ± 0.35; $n = 8$, see Table 1) and the astigmatic axis was ±15° from the horizontal or vertical meridian. Subjects were optically corrected. The lateral interactions in the meridian with the lower refractive error (smallest optical blur) and the meridian with the astigmatic error (higher optical blur) were measured and compared. Fig. 6 presents the results (mean ± SEM) for eight subjects measured at different spatial frequencies (mean spatial frequency ± SEM, 7.2 ± 0.8 cpd). As can be seen, spatial interactions are practically normal at the direction with the lower refractive error, while facilitation is poor along the orthogonal axis, where the refractive error is highest.

Table 1
Refractive information of the meridional amblyopic subjects

		Sph	Cyl	Axis	VA (LogMar)
AK	A	−9.25	−3.00	180	0.55
	NAE	Pl	−0.50	170	0.05
DK	A	3.50	−2.00	170	0.3
	NAE	0.75	−0.75	165	−.05
MS	A	−2.75	−2.25	180	0.48
	NAE	−2.50	−1.25	180	0.04
MH	A	3.25	−3.50	15	0.34
	NAE	0.75			−.04
MZ	A	−12.00	−1.50	85	0.5
	NAE	−.25	−.25	170	−.03
NR	A	5.50	−4.25	165	0.39
	NAE	−1.25			0.02
SK	A	3.00	−5.25	170	0.3
	NAE	0.25	−0.50	170	−.02
ZA	A	Pl	−1.50	180	0.36
	NAE	Pl			0

Refractive information of the meridional amblyopic subjects which their data is presented in Fig. 6 A = amblyopic eye, NAE = non-amblyopic eye, Sph = spherical power in diopters Cyl = cylinder power in diopters, Axis = the axis of the cylinder, VA = visual equity as measured on ETDRS chart (LogMar).

4. Discussion

The results presented here are consistent with results from previous experiments (Ellemberg et al., 2002; Bonneh, Sagi, & Polat, 2004; Levi et al., 2002; Polat et al., 1997) showing that spatial interactions in amblyopia are abnormal. Here we showed, in addition, that the anomalous spatial interactions are specific to certain combinations of parameters, namely spatial frequency, amblyopia type, and astigmatic axis. Thus, for a given set of parameters, some amblyopic patients might perform as well as normal subjects, while exhibiting significant abnormalities for other parameter combinations. Furthermore, the deficits observed were dependent also on the amblyopia type, strabismus or anisometropic, and within type on the details of the deficit, as in meridional amblyopia. The differences observed here between strabismic and anisometropic amblyopes are consistent with the increased effect of crowding found in strabismic but not anisometropic amblyopia (Bonneh et al., 2004). The crowding results indicate the existence of a specific non-local component of the strabismic deficit, in addi-

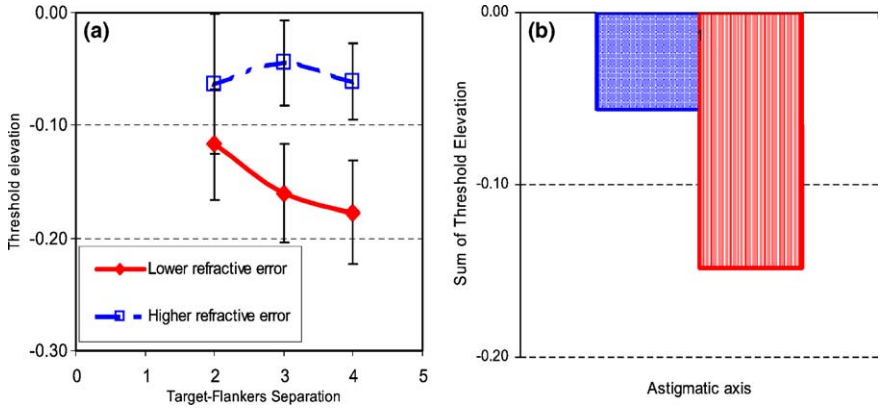

Fig. 6. Spatial interactions in meridional amblyopia. (a) Data (mean ± SEM) from eight anisometropic amblyopic subjects ($n = 8$, measured at 3 cpd) with meridional amblyopia. The refraction of each subject is depicted in Table 1. A comparison is shown between the lower refractive error axis (filled squares) and higher refractive error (open squares). In the less blurred axis the facilitation is as good as in subjects without amblyopia, whereas in the more blurred axis there is only slight facilitation. (b) Average of the threshold elevation values at 2λ, 3λ, and 4λ taken from each subject, as described in Fig. 2a. Facilitation is normal for the less blurred axis and subnormal for the more blurred axis.

tion to the local acuity deficit in all amblyopia types. This deficit might reflect long-range lateral inhibition, or alternatively, an inaccurate and scattered top-down attentional selection mechanism.

Amblyopic eyes commonly have reduced contrast sensitivity, particularly at high spatial frequencies (Gstalder & Green, 1971; Harwerth & Levi, 1977). It was suggested (Levi & Sharma, 1998) that degraded contrast sensitivity made the flankers used by Polat et al. (1997) less visible, and therefore less effective in the amblyopic eyes. This possibility appears to be supported by the present finding that the abnormality increased with increasing spatial frequency. However, it was shown (Ma-Naim, Ram, & Polat, 2000; Polat, 1999; Zenger & Sagi, 1996) that facilitation in normal subjects, at target–flanker distances of 3λ or more, is independent of flanker's contrast if that contrast is at least twice as high as the contrast threshold of the target. Levi et al. (2002) showed that collinear facilitation in amblyopic subjects, as in normal subjects, exists in both low and high flanker's contrast and thus is not dependent on the flanker's contrast. This result is not consistent with the idea that the abnormality in lateral interactions is due to the low visibility of the flankers resulting from abnormal contrast sensitivity function usually found in amblyopia. Moreover, although the abnormality in spatial interactions increases with increasing spatial frequency, the abnormal pattern of lateral interactions cannot be attributed to an anomalous contrast sensitivity in amblyopia, since the contrast thresholds of anisometropic and strabismic amblyopes was not significantly different, but their spatial interactions was significantly differ. Our present results are consistent with a recent study showing that spatial distortion increases with increasing spatial frequency (Barrett, Pacey, Bradley, Thibos, & Morrill, 2003).

Many anisometropic individuals have astigmatic refractive error. We showed here that in subjects with meridional amblyopia, spatial interactions might be abnormal in the more blurred axis and normal in the less blurred axis. All of our amblyopic subjects were tested on the best meridian first, and since this initial measurement of lateral interactions is the one presented here, the amount of abnormal spatial interactions might be an underestimation. It should be noted that both anisometropic and strabismic amblyopic individuals performed abnormally on the contour integration task of Kovács et al. (2000), in which there were circular contours consisting of Gabor patches with a wide range of orientations. On the other hand, Hess and Demanins (1998), using a path of Gabor patches that produced a quasi-linear contour in one global orientation, found almost normal contour detection in subjects with anisometropic amblyopia. It is possible that anisometropic subjects have more difficulty in detecting a circular target that incorporates their worse axis, making it difficult to trace the circular path, but have less difficulty in detecting a less curved target that does not coincide with their defective axis.

This study adds new information to the growing body of evidence for abnormal lateral interactions in amblyopia (Bonneh et al., 2004; Ellemberg et al., 2002; Levi et al., 2002; Polat et al., 1997). It is also consistent with the results of other experiments, demonstrating abnormal performance of amblyopic subjects in tasks requiring integration of global information (which might be mediated by spatial interactions), such as contour integration (Chandna et al., 2001; Hess & Demanins, 1998; Hess et al., 1997; Kovács et al., 2000), spatial localization (Popple & Levi, 2000), and spatial distortions (Lagreze & Sireteanu, 1991; Sireteanu, Lagreze, & Constantinescu, 1993). It is intriguing to speculate on what might account for the loss of spatial interactions in amblyopic subjects.

Traditionally, the abnormal spatial vision in amblyopia is explained in terms of abnormal local processing, caused either by reduction in the number of neurons (as a result of sampling) (Levi & Klein, 1986) or by disarray (jitter) of their spatial relationships (Hess & Field, 1994). An alternative view based on integrative processing (Polat, 1999; Polat et al., 1997) suggests that in individual with amblyopia, lateral interactions between the neurons that mediate spatial vision are compromised.

Recent findings confirming the observations that spatial interactions are abnormal in amblyopia (Ellemberg et al., 2002; Levi et al., 2002; Polat et al., 1997) raise questions about the interpretation of the finding of abnormal spatial interactions. Ellemberg et al. (2002) suggest that in amblyopic subjects the contrast response of a local target is not influenced by the surrounding targets and that amblyopes might have a normal contrast gain control but within a disturbed topographical representation. These authors suggest that "in this case the primary deficit would be the anomalous lateral interactions subserving positional coding of non-overlapping image features rather than anomalous lateral interactions subserving the contrast gain control mechanism per se." According to this view, there are two separate mechanisms of lateral interactions. It was shown, however, that collinearity improves spatial alignment, and therefore that collinear interactions is involved in positional coding (Popple, Polat, & Bonneh, 2001; Popple & Levi, 2002) thus being inseparable.

A recent study (Levi et al., 2002), does not share the conclusion of Polat et al. (1997) regarding abnormal long-range neural connections. The authors give several reasons for their different interpretation. First, they note that the finding is not general and that there is some variability in the data. In the present study we referred to several factors (such as spatial frequency, axis of astigmatism, and amblyopia type) that affect the facilitatory effect and might account for this variability. Another

possible reason for the variability has to do with the effects of perceptual learning that occur when normal and amblyopic subjects are trained in visual tasks (Levi & Polat, 1996; Levi, Polat, & Hu, 1997; Polat & Sagi, 1994b) or, as recently shown, in tasks of lateral interactions in amblyopic subjects (Bonneh et al., 2004; Polat et al., 2004). Another possible source that may contribute to the variability between amblyopic subjects may be the degree of the binocular loss (McKee, Levi, & Movshon, 2003) that yet is not taken in account in the recent studies.

The key argument of Levi et al. (2002) in support of an alternative interpretation is that the size of long-range connections in area V1 is about 1–2 mm, which is far too short to account for the effects seen psychophysically. Regardless of the length of the horizontal connections, it was suggested that long-range horizontal interactions can be established through cascades of (local) lateral connections, making it possible to convey signals over much longer distances than can be revealed by monosynaptic connections of the horizontal connections (Polat, 1999; Polat & Sagi, 1994b; Polat & Sagi, 1995). This view recently received support from the suggestion (Li & Gilbert, 2002) that "global contour saliency is based on local integration mechanisms of intermediate spatial extent, comparable to the interactions observed in collinear facilitation," and that "these interactions can cascade over very large distances as long as the spacing of stimulus elements is kept within a limited range." This view is strongly supported by the finding that sub-threshold signals, mediated by the long-range interactions, are propagated for very large distances in V1 (Bringuier, Chavane, Glaeser, & Fregnac, 1999; Grinvald, Lieke, Frostig, & Hildesheim, 1994). Taken together with recent anatomical (Stettler, Das, Bennett, & Gilbert, 2002) and the functional results that discussed above, intrinsic horizontal connections in V1 are likely to provide a substrate for spatial interactions such as collinear facilitation and suppression.

The increasing body of evidence suggesting that integrative mechanisms are compromised in amblyopic subjects seems to converge to an agreement about the abnormal functionality of spatial interactions in amblyopia. There are still different views, however, about whether the underlying abnormality relies on abnormal neural interactions (Ellemberg et al., 2002; Polat et al., 1997) or is due to an attentional abnormality that contributes to uncertainty (Levi et al., 2002). Furthermore, given the deviation of the results between the amblyopic types, different models may account for the different amblyopia types. As of today, none of these explanations can be absolutely ruled out, and experiments designed to target each of the above predictions will be required in order to achieve a better understanding of the nature of the abnormal lateral interactions in individuals with amblyopia. All explanations need to account for the developmental aspect of amblyopia, that abnormal lateral interactions are a result of specific distortions in the visual input experienced by a subject during the developmental period.

Acknowledgments

This study was supported by grants to U. Polat and Y. Bonneh from the National Institute for Psychobiology in Israel founded by The Charles E. Smith Family, and by NeuroVision Inc.

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